Abstract

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Abstract: *DESCRIPTION (provided by applicant):* G-protein coupled receptors (GPCRs), ion channels, and transporters are areas of intense basic research and are proven drug targets. However, there remains a need for new tools to develop a better understanding of the roles of these proteins in biological systems and to pave the way for discovery of therapeutic agents. Although ligand discovery has been performed on these proteins in pharmaceutical companies, their retail product interests often preclude, or greatly delay, the publication of research findings or consider only one of the many possible modes of target/small molecule interaction. Despite intense interest of multiple academic and industry labs, small molecules ligands do not exist for the vast majority of GPCRs, ion channels, and transporters. The research community, supported by the Molecular Libraries and Screening Centers Network (MLSCN) initiative, has an excellent opportunity to develop novel tools to aid in understanding these proteins. Thus, we propose to develop a MLSCN screening center focused on the generation of chemical tools for the study of G-protein coupled receptors, ion channels, and transporters. We will perform cell-based functional HTS for these proteins using industry-standard instrumentation and screening methods. We will further enhance our ability to rapidly discover and characterize novel tools for these targets and the signaling pathways/physiological systems of which they are a part by using new technologies that will allow more physiologically-relevant interrogation of interactions between these proteins and their partners. We will develop the expertise, technologies, and methods to understand and improve the properties of small molecules discovered through HTS to produce tools to support basic and translational research. Vanderbilt University is well suited to support an MLSCN center due to its combination of basic and industrial research expertise in the proposed target areas, its dedication to translational and chemical biology, and its tradition of excellence in the establishing and maintaining highly-collaborative laboratories and core facilities.